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(54) HOLLOW FIBER MEMBRANE FOR HEMATOCATHARSIS AND HOLLOW FIBER MEMBRANE TYPE ARTIFICIAL KIDNEY

(57)Abstract:
PROBLEM TO BE SOLVED: To provide a hollow fiber membrane for hematocatharsis and a hollow fiber membrane type artificial kidney in which endotoxine is adsorbed on an outer surface and to provide a hollow fiber membrane for hematocatharsis and a hollow fiber membrane type artificial kidney in which a hydrophilic polymer in the hollow fiber membrane is less and a blood platelet is not adsorbed.
SOLUTION: In the hollow fiber membrane prepared from a membrane- forming stock solution in which a hydrophilic polymer and a hydrophobic polymer are solvent and mixed in a common solvent, a hollow fiber membrane for hematocatharsis in which a ratio of the hydrophilic polymer is used against the hydrophobic polymer on an outer surface of the hollow fiber membrane is 5-25%.

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CLAIMS

[Claim(s)]
[Claim 1] The hollow fiber for blood purification characterized by the ratio of the hydrophilic macromolecule to the hydrophobic macromolecule in the outside surface of this hollow fiber being 5 - 25% in the hollow fiber manufactured from the film production undiluted solution which made the common solvent carry out dissolution mixing of a hydrophilic macromolecule and the hydrophobic macromolecule.
[Claim 2] The hollow fiber for blood purification according to claim 1 characterized by said hydrophobic macromolecule being polysulfone system resin.
[Claim 3] The hollow fiber for blood purification according to claim 1 or 2 characterized by being chosen out of the group which said hydrophilic giant molecule becomes from a polyvinyl pyrrolidone, a polyethylene glycol and its copolymer, a polypropylene glycol, and its copolymer.
[Claim 4] Claim 1 characterized by carrying out coating of the anti-thrombus nature matter to the internal surface of said hollow fiber thru/or the hollow fiber for blood purification given in 3.
[Claim 5] Claim 1 characterized by said anti-thrombus nature matter being vitamin E thru/or the hollow fiber for blood purification given in 4.
[Claim 6] The hollow fiber mold artificial kidney which has the hollow fiber indicated by claim 1 thru/or 5.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to the hollow fiber for blood purification and hollow fiber mold artificial kidney which are used for a blood purification therapy especially a hemodialysis therapy, and hemofiltration dialysis. In more detail, while preventing invasion of the endotoxin from a dialysing fluid side, it is related with the hollow fiber for blood purification and hollow fiber mold artificial kidney which suppressed adsorption of a platelet in the blood contact surface.
[0002]
[Description of the Prior Art] The various artificial kidneys which used the current hollow fiber for the renal failure therapy are used. In recent years, it is shown that removal of with a molecular weight of 10,000 or more which made beta 2-microglobulin one index low-molecular-weight protein is effective in a therapy, and development of the blood purification film which has the fine hole which can pass low-molecular-weight protein has been performed briskly. Furthermore, in order to remove low-molecular-weight protein positively, coincidence hemofiltration dialysis which combined hemodialysis and hemofiltration is performed.
[0003] However, if the magnitude (pore size) of a membranous fine hole is expanded in order to remove low-molecular-weight protein since the dialysing fluid which flows the opposite side on both sides of the film flows into a blood side in the case of the above-mentioned therapy, possibility that the endotoxin (endotoxin) contained in dialysing fluid will invade into a blood side increases, and we are anxious about causing side effects, such as generation of heat.
[0004] Endotoxin has a hydrophobic part, it is known that it will be easy to stick to a hydrophobic ingredient, and the endotoxin removal filter using this principle is developed. JP,10-151196,A and JP,10-118472,A produce a hollow fiber only from a hydrophobic macromolecule, and are making endotoxin adsorb. In order to make the fall of the permeable ability by a hydrophobic macromolecule tending [furthermore] to adsorb the protein in blood improve, the hydrophilic macromolecule is made to adhere only to a hollow filament inside. In these applications, a film production undiluted solution is not made to mix a hydrophilic macromolecule, but hydrophilization processing of the internal surface is carried out after film production noting that hydrophobing of a film outside surface is impossible, if a hydrophilic macromolecule exists in a film production undiluted solution.
[0005] By the Prior art, pinpointing the suitable range was not shown by giving a hydrophilic macromolecule to the hollow fiber which consists of a hydrophobic macromolecule, taking adjustment with the fall of the adsorption capacity force of the endotoxin by that permeable ability improves and the hydrophilic property of a hollow fiber increasing.
[0006] Moreover, after adding a hydrophilic macromolecule to the film production undiluted solution of a hydrophobic macromolecule and producing a film to it, when decreasing the amount of the hydrophilic macromolecule of an outside surface by washing etc., the amount of hydrophilic macromolecules of the front face in contact with blood also decreases, and it is indicated by JP,6-296686,A that adhesion of a platelet etc. arises.
[0007]
[Problem(s) to be Solved by the Invention] The purpose of this invention is in the hollow fiber produced from the film production undiluted solution with which the hydrophilic macromolecule which

solved the above-mentioned problem, and the hydrophobic macromolecule were mixed to offer the hollow fiber for blood purification and hollow fiber mold artificial kidney which adsorb endotoxin to an outside surface.
[0008] Furthermore, the purpose of this invention has a hydrophilic macromolecule in a hollow fiber in offering the hollow fiber for blood purification and hollow fiber mold artificial kidney to which a platelet is not made to stick few.
[0009]
[Means for Solving the Problem] Many above-mentioned purposes are attained by the following hollow fibers for blood purification and hollow fiber mold artificial kidneys of this invention.
[0010] (1) The hollow fiber for blood purification characterized by the ratio of the hydrophilic macromolecule to the hydrophobic macromolecule in the outside surface of this hollow fiber being 5 - 25% in the hollow fiber manufactured from the film production undiluted solution which made the common solvent carry out dissolution mixing of a hydrophilic macromolecule and the hydrophobic macromolecule.
[0011] (2) The hollow fiber for blood purification given in (1) characterized by said hydrophobic macromolecule being polysulfone system resin.
[0012] (3) (1) characterized by being chosen out of the group which said hydrophilic giant molecule becomes from a polyvinyl pyrrolidone, a polyethylene glycol and its copolymer, a polypropylene glycol, and its copolymer, or the hollow fiber for blood purification given in (2).
[0013] (4) The claim (1) characterized by carrying out coating of the anti-thrombus nature matter to the internal surface of said hollow fiber thru/or the hollow fiber for blood purification given in (3).
[0014] (5) (1) characterized by said anti-thrombus nature matter being vitamin E thru/or the hollow fiber for blood purification given in (4).
[0015] (6) The hollow fiber mold artificial kidney which has the hollow fiber indicated by the above (1) thru/or (5).
[0016]
[Embodiment of the Invention] This invention is explained to a detail below.
[0017] Polymethylmethacrylate, polystyrene, polysulfone, cellulose triacetate, a polycarbonate, polyarylate, etc. are mentioned, and the hydrophobic giant molecule which forms the hollow fiber for blood purification of this invention may be used combining these independence or two sorts or more. These hydrophobic macromolecules can prevent the invasion by the side of the blood of the endotoxin from a dialysing fluid side, when it has endotoxin adsorbent and it is used as an artificial kidney.
[0018] The hollow fiber for blood purification of this invention receives fixed washing processing in the film production undiluted solution after film production including a hydrophilic macromolecule, and remains in a hollow fiber. The hydrophilic giant molecule used for this invention contains the copolymer containing polymers, such as polyvinyl alcohol, a polyethylene glycol, a polypropylene glycol, a polyvinyl pyrrolidone, and polytetramethylene oxide, or these. A polyvinyl pyrrolidone is preferably desirable in respect of the ease of film production nature and aperture control. Moreover, 5 million dalton of desirable weight average molecular weight is 30,000 to 2 million dalton more preferably from 10,000. The aperture control for making it function as permeable membrane is easy.
[0019] 5 to 25% of the ratio to the hydrophobic macromolecule of the hydrophilic macromolecule by the side of the dialysing fluid which remains in the hollow fiber for blood purification of this invention (usually outside surface of a hollow fiber) is desirable. If it is this range, the endotoxin contained in dialysing fluid can be made to adsorb effectively. It is 5 to 20% more preferably. The ratio to the hydrophobic macromolecule of the hydrophilic macromolecule by the side of dialysing fluid says the rate of an abundance ratio of this hydrophilic macromolecule and this hydrophobic macromolecule measured with measuring methods, such as X-ray photoelectron spectroscopy (X-ray photoelectron spectroscopy, XPS), infrared spectroscopy, and a nuclear magnetic resonance method. For example, when a polyvinyl pyrrolidone (PVP) is chosen as polysulfone resin (PS) and a hydrophilic giant molecule as a hydrophobic giant molecule, the ratio of the total atomic weight of PS which exists in a hollow fiber front face, and each PVP can be computed and calculated by XPS from the sulfur (PS) and the element ratio of nitrogen (PVP) which are a characteristic element, and the repeat unit molecular weight of PS and PVP.
[0020] Moreover, the ratio of the hydrophilic macromolecule to the hydrophobic macromolecule of the

whole hollow fiber of this invention has 1.0 to 6.0 desirable % of the weight. It is 2.0 to 5.0 % of the weight more preferably. Washing actuation must be performed superfluously and effectiveness is bad at below a lower limit. Moreover, above a upper limit, the ratio of a hydrophilic macromolecule will rise rapidly toward the interior of the film from a hollow fiber outside surface, the field to which endotoxin sticks decreases, and it is not desirable. The ratio of the hydrophilic macromolecule of the whole hollow fiber has the approach of dissolving a hollow fiber in a solvent and analyzing by NMR etc., an approach by elemental analysis, etc. For example, when a polyvinyl pyrrolidone is used as polysulfone and a hydrophilic giant molecule as a hydrophobic giant molecule, a weight ratio can be calculated from the nitrogen and the sulphuric element ratio by elemental analysis, and the molecular weight of the repeat unit of each giant molecule.

[0021] When producing a hollow fiber, the wet spinning approach or the dryness-and-moisture type spinning approach used conventionally can be used. When performing these spinning approaches, said hydrophobic macromolecule and hydrophilic macromolecule are dissolved in these common solvents, and a film production undiluted solution is adjusted. As this common solvent, although solvents, such as N,N-dimethylacetamide, N.N-dimethylformamide, N-methyl pyrrolidone, and dimethyl sulfoxide, are highly suitable for solubility, it is not limited to these, and two or more sorts of solvents may be mixed, and you may use. It is the point of the ease of acquisition preferably and N,N-dimethylacetamide and N.N-dimethylformamide are used independently.

[0022] Moreover, in order to tune viscosity accommodation, aperture control, etc. finely to a film production undiluted solution, optimum dose addition of alcohol, a glycerol, the water, etc. may be carried out. The point of effluent processing to water is desirable, and 0.1 to 5 % of the weight is desirable to the above-mentioned fine tuning in a film production undiluted solution.

[0023] When too low, film reinforcement is small, the concentration of the hydrophobic macromolecule in a film production undiluted solution must perform spinning activity and assembly operation carefully, and its effectiveness is bad. Moreover, if concentration is too high, the viscosity of a film production undiluted solution will rise, the film becomes precise, and the conditioning of the required aperture **** sake as an artificial kidney is difficult. When polysulfone is used as a hydrophobic macromolecule, the concentration in the film production undiluted solution of a desirable hydrophobic macromolecule is 15 to 19 % of the weight still more preferably 25% of the weight in 12 preferably 30% of the weight from 10. Since a desirable density range is changed with the class of hydrophobic macromolecule, molecular weight, etc. in a detail, it is not limited to this range.

[0024] If the concentration of the hydrophilic macromolecule in a film production undiluted solution is too low, good aperture control will become difficult, if too high, the viscosity of a film production undiluted solution will rise and spinning nature will get worse. When the polyvinyl pyrrolidone of weight-average-molecular-weight 45,000 Dalton is used as a hydrophilic giant molecule, the concentration in a desirable film production undiluted solution is 7 to 10 % of the weight more preferably 15% of the weight from 5. Concentration low when what has high molecular weight is used is sufficient, and high concentration is desirable when what has low molecular weight is used.

[0025] As internal liquid which carries out the regurgitation from the inner tube of a double pipe nozzle, the mixture of the above-mentioned common solvent and water is mainly used in the case of wet spinning or dryness-and-moisture type spinning. What mixed two or more sorts of above-mentioned common solvents for control of the coagulation rate of a film production undiluted solution, and other liquids may be mixed.

[0026] It is immersed in the coagulation bath to which the film production undiluted solution breathed out from the double pipe nozzle made water the subject. a film production undiluted solution -- a coagulation bath -- as a hollow fiber -- firmly -- form attachment ****. Then, if needed, it is immersed in a wash bath and rinses. PVP of an outside surface is washed, so that the temperature of a wash bath is high. In order to adjust PVP of the outside surface of a hollow fiber into a desirable ratio, it is desirable to make temperature of a wash bath into 40 to 80 degrees C. It is desirable to wash especially at 50 to 70 degrees C. Since to move in the perimeter of a hollow fiber is [washing effectiveness] higher, the wash water of this wash bath circulates wash water, and may be used. Under the present circumstances, since the PVP concentration in wash water becomes high gradually and washing effectiveness falls during circulation, it is desirable to supply always new wash water. It is desirable that the amount of the new wash water supplied in 1 hour is 10 to 50 of a wash water total

amount%.
[0027] The hollow fiber washed by the wash bath can wash PVP of a hollow fiber outside surface positively by performing rolling up and washing with the mixed solution of warm water, alcohol, alcohol, and water etc. further. Thus, the endotoxin adsorption capacity to an outside surface is obtained from 5 by considering as 5 to 20% preferably 25% in the rate of an abundance ratio of the hydrophilic macromolecule of the outside surface of the obtained hollow fiber. Water permeability decreases that the rate of an outside-surface abundance ratio of a hydrophilic macromolecule is less than 5%. If the rate of an outside-surface abundance ratio of a hydrophilic macromolecule exceeds 25%, the hydrophilic property of an outside surface will become high and the adsorption capacity of endotoxin will fall.
[0028] Moreover, as for the hollow fiber for blood purification of this invention, it is desirable to give the anti-thrombus nature matter in order to control platelet adhesion of the hollow filament internal surface in contact with blood. It is because the rate of an abundance ratio of the hydrophilic macromolecule of an internal surface also falls and a platelet becomes easy to adhere, when the rate of an abundance ratio of the hydrophilic macromolecule of a hollow fiber outside surface is made into 5 to 25%. With the anti-thrombus nature matter, fat soluble vitamins, such as long-chain unsaturated fatty acid, such as a polymeric material which has a hydrophilic part like a styrene-hydroxyethyl methacrylate copolymer and the polymer of the acrylic-acid system monomer which has a hydrophilic group (meta), and the acrylic-acid system monomer which has a hydrophobic group (meta), and a hydrophobic part, eicosapentaenoic acid, and docosa-hexaenoic acid, and vitamin E, are mentioned. The point that the stability over the ease and heat of processing is high to vitamin E is desirable. As vitamin E, the alpha-tocopherol, the beta-tocopherol, the gamma-tocopherol, delta-tocopherol, alpha-tocopherol acetate, alpha-tocopherol nicotinate, etc. are mentioned.
[0029] (Example 1) The homogeneity dissolution of 19 % of the weight (P-1700) of polysulfones, 9 % of the weight (K-30) of polyvinyl pyrrolidones, and the 72 % of the weight of the N.N-dimethylformamide was carried out, and the film production undiluted solution was adjusted. Internal liquid used 60 % of the weight of N.N-dimethylformamide, and the mixed liquor of 40 % of the weight of water.
[0030] The coagulation bath with which discharge and water were filled by coincidence in air from the outer tube and inner tube of a double tubing regurgitation nozzle in an above-mentioned film production undiluted solution and internal liquid, respectively was passed. After passing a coagulation bath, shower washing of the 60-degree C warm water was carried out by part for 1L/for 1 hour.
[0031] After shower washing, the hollow fiber was rolled round and it was made 10,000 bundles, and it processed underwater for 110 more degree-C 1 hour, and washed.
[0032] (Example 2) The homogeneity dissolution of 19 % of the weight (P-1700) of polysulfones, 9 % of the weight (K-30) of polyvinyl pyrrolidones, and the 72 % of the weight of the N.N-dimethylformamide was carried out, and the film production undiluted solution was adjusted. 0.1% of the weight of alpha-tocopherol acetate and 0.1% of the weight of a polyethylene-glycol-polypropylene-glycol copolymer (Pluronic F-68, Asahi Denka Kogyo K.K. make) were added and used for internal liquid to 60 % of the weight of N.N-dimethylformamide, and the mixed liquor of 40 % of the weight of water.
[0033] The coagulation bath with which discharge and water were filled by coincidence in air from the outer tube and inner tube of a double tubing regurgitation nozzle in an above-mentioned film production undiluted solution and internal liquid, respectively was passed. After passing a coagulation bath, shower washing of the 60-degree C warm water was carried out by part for 1L/for 1 hour.
[0034] After shower washing, the hollow fiber was rolled round and it was made 10,000 bundles, and it processed underwater for 110 more degree-C 1 hour, and washed.
[0035] (Example 1 of a comparison) The homogeneity dissolution of 19 % of the weight (P-1700) of polysulfones, 9 % of the weight (K-30) of polyvinyl pyrrolidones, and the 72 % of the weight of the N.N-dimethylformamide was carried out, and the film production undiluted solution was adjusted. internal liquid -- 60 % of the weight of N.N-dimethylformamide, and 40 % of the weight of water -- mixed liquor was carried out and it used.
[0036] The coagulation bath with which discharge and water were filled by coincidence in air from the outer tube and inner tube of a double tubing regurgitation nozzle in an above-mentioned film production undiluted solution and internal liquid, respectively was passed. After passing a coagulation bath, shower washing of the 60-degree C warm water was carried out for 10 minutes by part for 1L/.

[0037] (Example 2 of a comparison) The homogeneity dissolution of 19 % of the weight (P-1700) of polysulfones, 1 % of the weight (K-30) of polyvinyl pyrrolidones, and the 80 % of the weight of the N.N-dimethylformamide was carried out, and the film production undiluted solution was adjusted. internal liquid -- 60 % of the weight of N.N-dimethylformamide, and 40 % of the weight of water -- mixed liquor was carried out and it used.
[0038] The coagulation bath with which discharge and water were filled by coincidence in air from the outer tube and inner tube of a double tubing regurgitation nozzle in an above-mentioned film production undiluted solution and internal liquid, respectively was passed. After passing a coagulation bath, shower washing of the 60-degree C warm water was carried out by part for 1L/for 1 hour.
[0039] After shower washing, the hollow fiber was rolled round and it was made 10,000 bundles, and it processed underwater for 110 more degree-C 1 hour, and washed.
[0040] The rate of an abundance ratio of the polyvinyl pyrrolidone of the outside surface of the hollow fiber obtained in examples 1 and 2 and the examples 1 and 2 of a comparison was measured by XPS, the hollow fiber mold artificial kidney of 2 was produced 1.5m of effective film surface products using housing which has further the inside of a hollow fiber, a blood inlet port open for free passage, a blood outlet, and the dialysing fluid inlet port which is open for free passage the external surface side of a hollow fiber and a dialysing fluid outlet, and permeable ability and endotoxin adsorption capacity were measured. A measurement result is shown in Table 1.
[0041] Measurement of permeable ability filtered Milli Q water by rate-of-flow 15 ml/min from the external surface of a hollow fiber using the above-mentioned hollow fiber mold artificial kidney by supplying water by rate-of-flow 200 ml/min inside a hollow fiber, and measured and computed the differential pressure between film at that time.
[0042] Measurement of the adsorption capacity of endotoxin was performed using the above-mentioned hollow fiber mold artificial kidney as follows. The dialysing fluid which sent the dialysing fluid of endotoxin concentration 800 EU/L by rate-of-flow 30 ml/min from the dialysing fluid inlet port, controlled the flow from a dialysing fluid outlet to 5 ml/min using the pump, filtered the dialysing fluid which contains endotoxin from the external surface side of a hollow fiber to the inside positively for 4 hours, and was filtered from the outside of a hollow fiber in the inside of a hollow fiber was stored, and the endotoxin concentration of this reservoir liquid was measured. Test fluid was not recycled but circulated only to the one direction.
[0043]
[Table 1]

	膜全体のPVP比率 (%)	PVP外表面比率 (%)	透水性能 (ml/mmHg・hr)	エンドトキシン濃度 (EU／L)
実施例1	2．8	17	490	検出限界以下
実施例2	2．3	14	470	検出限界以下
比較例1	6．7	30	460	8
比較例2	0．8	3	20	検出限界以下

検出限界：1EU／L

[0044] As Table 1, examples 1 and 2 have permeable ability equivalent to the example 1 of a comparison, and have the adsorption capacity of endotoxin. On the other hand, as for the example 1 of a comparison, endotoxin was detected by reverse filtration of dialysing fluid of 4 hours to the blood side. Moreover, although the endotoxin by the side of blood was not detected for the example 2 of a comparison, permeable ability decreased prominent.
[0045] (Example 3) Polymer concentration was diluted with the methanol for 30% methyl-isobutyl-ketone solution of polymer concentration of the random copolymer (polymer 1) of hydroxyethyl methacrylate, methyl methacrylate, and butyl methacrylate, and the block copolymer (the ratio of polymers 1 and 2 is the weight ratio 50:50 and a mean molecular weight 35,000) of polyperfluoro alkyl methacrylate (polymer 2) to 0.7%. After dipping this solution in PS film inside of an example 1, the

solvent was removed by 50-degree C desiccation, and the polymer was coated on PS film.
[0046] The permeable ability of the artificial kidney of 2 was 320 ml/mmHg-hr 1.5m of effective film surface products in the obtained hollow fiber.
[0047] (Aging of a platelet count) The mini module of 2 was produced 300cm of film surface products using the hollow fiber obtained in the example 1, the example 2, and the example 3.
[0048] Twice many Nembutal eating-raw-food [as this] diluent 1 ml/kg was injected intravenously and anesthetized using the rabbit (weight of 2.7-3.3kg). The rabbit was fixed to standing ways, the blood vessel of a neck condition pulse was secured, and it circulated for 2 hours, without connecting a circuit and a mini module and using an anticoagulant by blood stream QB=10 ml/min. Blood collecting was performed from the artery side blood collecting port of a mini module, and aging of a platelet count was measured. In addition, the rate of change of a platelet was amended with the hematocrit value (bottom type).
[0049]
[Equation 1]

$$\text{血球変化率} = \frac{PL_t \times Ht_0}{PL_0 \times Ht_t} \times 100\%$$

PL_0：循環前の血球数、Ht_0：循環前のヘマトクリット値

PL_t：循環t時間の血球数、Ht_t：循環t時間のヘマトクリット値

[0050] A result is shown in Table 2.
[0051]
[Table 2]

時間(分)	実施例1	実施例2	実施例3
0	100	100	100
5	90.1	93.5	89.7
10	89.1	90.8	86.0
15	83.8	90.4	84.6
20	81.9	87.2	85.7
25	79.9	86.7	84.3
30	75.1	85.5	84.9
45	65.5	84.0	83.3
60	61.6	80.9	81.6
120	57.5	84.8	81.3

[0052] (Measurement of erythrocyte membrane MDA) The following actuation was performed using the mini module of the example 1 of 2, and an example 2 600cm of film surface products.
[0053] First, the priming of the 50ml of the sterilized mini modules was carried out by eating raw food, the mini module was filled up with 10U/ml heparinized blood, and it incubated at 37 degrees C for 6 hours. Then, blood was collected from the mini module and the number of red cell was counted by the corpuscle computer (Sysmex SE9000 and TOA Medical Electronics Co., Ltd.) (red blood cell count). Moreover, the erythrocyte which removed plasma according to plasma skimming (3,000rpm, 15min, 4 degrees C), and precipitated to 10mM PBS(pH8.0)5.4ml in 1.8ml (finishing [a red blood cell count]) of blood collected from the mini module was made to suspend, centrifugal separation (3,000rpm, 15min, 4 degrees C) was carried out, and PBS of supernatant liquid was removed and washed. After performing this washing actuation a total of 3 times, PBS of supernatant liquid was removed, 5mMPBS(pH8.0) 5.4ml was added, and the erythrocyte was hemolyzed.
[0054] PBS of supernatant liquid is removed, and 2.5mMPBS(s)(pH8.0)5.4ml is mixed to an erythrocyte, and it is made to carry out centrifugal separation (10,000rpm, 15min, 4 degrees C) of the above-mentioned sample which carried out hemolysis, and to hemolyze. Furthermore centrifugal separation (10,000rpm, 15min, 4 degrees C) was carried out, PBS of supernatant liquid was removed, it mixes to an erythrocyte, it was hemolyzed and centrifugal separation (10,000rpm, 15min, 4 degrees C) of the 1.25mMPBS(s)(pH8.0)5.4ml was carried out. Hemolysis by 1.25mMPBS(s), centrifugal separation, and

washing actuation are repeated a total of 5 times. After removing PBS of supernatant liquid finally, the whole quantity was doubled with 2ml by 1.25mMPBS.
[0055] MDA (malondialdehyde) was measured for the erythrocyte membrane obtained by the above-mentioned preparation by the TBA method as a sample (peroxylipid Test Wako: Wako Pure Chem industrial company make). Operating instructions are shown below.
[0056] A result is shown in Table 3.
[0057]
[Table 3]
赤血球過酸化脂質 (n=5)

	MDA nmol／10^{10}RBC
PRE	3. 507
実施1	6. 701
実施2	5. 558

[0058] By coating a hollow fiber inside side with the anti-thrombus nature matter shows that reduction in a platelet can be controlled. Moreover, when vitamin E is used, it turns out that peroxidation of an erythrocyte membrane lipid can be controlled.
[0059]
[Effect of the Invention] This invention can obtain the hollow fiber for blood purification and hollow fiber mold artificial kidney which adsorb endotoxin to an outside surface in the hollow fiber produced from the film production undiluted solution with which the hydrophilic macromolecule and the hydrophobic macromolecule were mixed as explained above.
[0060] Furthermore, this invention can obtain the hollow fiber for blood purification and hollow fiber mold artificial kidney to which the hydrophilic macromolecule in a hollow fiber does not make a platelet stick few.

[Translation done.]